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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,101	11/03/2006	Norio Teramae	118097-002	4072

24573 7590 05/12/2009

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EXAMINER
PANDE, SUCHIRA

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,101	TERAMAE ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-26* is/are pending in the application.

4a) Of the above claim(s) *21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/19/06 and 11/12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to comply with Sequence rules*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I (method) in the reply filed on April 23, 2009 is acknowledged. Examiner had done Lack of Unity for claims 1-11 that were pending. Applicant has cancelled all previously pending claims (1-11) and added new claims 12-26. Of these, new claims 12-20 are drawn to method. Hence consonant with above election claims 12-20 will be examined in this action.

2. Claims 21-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group II invention (product claims (kit)).

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Applicant claims priority to Japanese Application 2004-080703 filed in Japan on 2004-03-19 and has provided a certified copy of Japanese document. However no English translation has been provided, for prior art purposes Examiner is considering the priority of instant National Stage Application to be that of the filing date of PCT/JP05/006405 i.e. 18 March 2005.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 9/19/2006 and 11/12/2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

Sequence Rules Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is given time of reply to this office action within which to comply with the sequence rules, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in **abandonment** of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Pages 16, 18, 20 and 23 respectively contain sequences without corresponding SEQ ID NOs. No Sequence Listing has been provided by Applicant. The specification should be amended to include the SEQ ID NOs. Applicant should provide a sequence listing and a CRF that include those sequences along with the statement that the sequences in the sequence listing and CRF are identical.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 12-14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshimoto et al. (July 4, 2003) J. Am. Chem. Soc. 125 pp 8982-8983 (provided by Applicant in IDS).

Regarding claim 12, Yoshimoto et al. teach a method for detecting a gene mutation (see page 8983 par. 3 where detection of AP (abasic site) is taught. By teaching detection of AP site, Yoshimoto et al. teach a method for detecting a gene mutation) comprising:

forming a double-stranded nucleic acid (see fig. 1 right side where forming a double-stranded nucleic acid is shown) from:

(i) a single-stranded target nucleic acid having a target base composed of one or more continuous bases and two partial sequences thereof with the target base there between (see DNA single strand shown on left of Fig. 1 that meets all the recited characteristics. Examiner is referring to this strand as strand 1);

(ii) two single-stranded detecting nucleic acids complementary to the two partial sequences with the target base there between (see the strand containing AP site here the part on right and left side of AP site correspond to the two single-stranded detecting nucleic acids complementary to the two partial sequences. Examiner is referring to them

as strands 2a—top half (strand from top to base that is 5' of AP site) and 2b (strand from base that is 3' to AP site) bottom half. In between the two single strands 2a and 2b is the AP site linker. See duplex formed on right where location of target base is shown. The target base is present on the strand 1 between the two partial single strands 2a and 2b, thus Yoshimoto et al. teach two single-stranded detecting nucleic acids complementary to the two partial sequences with the target base there between);

forming a hydrogen bond by the target base and a receptor by inserting a receptor having hydrogen bonding characteristics into the double-stranded nucleic acid (see Fig. 1 where receptor is shown. Also see page 8982 par. 2 where use of 2-amino-7-methylnaphtyridine (AMND) to recognize AP site and forming hydrogen bond with the base opposite the Ap site is taught. Thus Yoshimoto et al. teach forming a hydrogen bond by the target base and a receptor by inserting a receptor having hydrogen bonding characteristics into the double-stranded nucleic acid); and

identifying the gene mutation where the receptor bonds to the target base (see fig. 4 where sequences differing in single nucleotides G, C, A, or T at the target site Y shown in oligo listed in figure legend of Fig. 4 are identified based on the fluorescence pattern of the duplex DNA formed which is observed using 302 nm UV lamp. See fig. 3 where binding of receptor AMND with target base C is shown. Thus Yoshimoto et al. teach identifying the gene mutation where the receptor bonds to the target).

Regarding claim 13, Yoshimoto et al. teach wherein the receptor has a heterocyclic aromatic group and is stabilized by the formation of a hydrogen bond to the target base and a stacking interaction with the base adjacent to the receptor to form a

pair with the target base (see Table 1 on page 8982 where structure of AMND = receptor of instant claim is shown. The structure of AMND shown has a heterocyclic aromatic group. See page 8982 col. 2 par. 1 where determination of stability between AMND and C indicates the significant role of stacking of AMND with nucleobases flanking the AP site is taught. Also see last line of this par. where conclusion is stated. " Therefore, AMND should bind to C in cooperative fashion, that is, hydrogen bonding with C and stacking with nucleobases flanking the AP site". Thus Yoshimoto et al. teach wherein the receptor has a heterocyclic aromatic group and is stabilized by the formation of a hydrogen bond to the target base and a stacking interaction with the base adjacent to the receptor to form a pair with the target base).

Regarding claim 14, Yoshimoto et al. teach wherein the receptor is at least one of a naphthylidine derivative, a quinoline derivative, a pteridine derivative, a coumarin derivative, an indazol derivative, an alloxazine derivative and amyloride (see page 8982 par. 2 where AMND taught is a methyl napthyridine hence teaching wherein the receptor is a naphthylidine derivative).

Regarding claim 18, Yoshimoto et al. teach wherein the receptor shows fluorescence emitting characteristics and the gene mutation is identified as a change of fluorescence strength of the double-stranded nucleic acid into which the receptor is inserted (see fig. 4 where the receptor shows fluorescence emitting characteristics and the gene mutation is identified as a change of fluorescence strength of the double-stranded nucleic acid into which the receptor is inserted).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 15-17 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshimoto et al. as applied to claim 12 above, and further in view of Nakatani et al. (2001) J. Am. Chem. Soc. 123: 12650-12657 (provided by Applicant in IDS).

Regarding claim 15, Yoshimoto et al. teach method of claim 12, and also teach that the double-stranded nucleic acid is formed by dropping on the substrate the single-stranded target nucleic acid and the two single-stranded detecting nucleic acids (based on teaching of Fig. 1 of Yoshimoto et al. it is obvious to one of ordinary skill in the art that when all the components required to form the duplex recited in claim 12 are present

in conditions taught by Yoshimoto et al. that lead to formation of duplex, the hybridization of two single strands corresponding to 2a and 2b along with strand 1 and binding of receptor AMND will take inherently take place.

Regarding claim 15 Yoshimoto et al. do not teach wherein the receptor is fixed to a substrate.

Regarding claim 15, Nakatani et al. teach wherein the receptor is fixed to a substrate (see page 12651 col. 2 par. 2 where naphtyridine derivative referred as compound 2 is immobilized onto dextran coated gold surface to develop a mismatch detecting sensor useful for a surface Plasmon resonance (SPR) assay.

Regarding claim 16, Nakatani et al. teach wherein the gene mutation is identified on the basis of the change of a signal strength of a surface plasmon resonance due to the bond of the target base and the receptor (see page 12651 col. 2 par. 2 where a mismatch detecting sensor useful for a surface plasmon resonance (SPR) assay is described. They go on to teach differentiation of 652 bp of PCR products of a G/C heterozygote from those of a G/G homozygote of HSP70-2 gene regarding the base at a nucleotide number 2345. Thus teaching Nakatani et al. teach wherein the gene mutation is identified on the basis of the change of a signal strength of a surface plasmon resonance due to the bond of the target base and the receptor).

Regarding claim 17, Yoshimoto et al. teach method of claim 12. Further as described above for claim 15, Nakatani et al. teach development of sensor where a component of the reaction mix namely receptor is fixed on substrate to develop sensor that is suitable for surface plasmon resonance (SPR) assay.

In the instant claims (15 and 17) applicant recites fixing a different component of the assay namely one detecting nucleic acid to a substrate instead of the fixing the receptor as taught by Nakatani et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Nakatani et al. in the method of Yoshimoto et al. to fix any of the components either the receptor or the one detecting nucleic acid to a substrate to form the sensor and then add the remaining components required to form the double stranded hybrid (claims 15 and 17). Thus Nakatani et al. teach wherein one detecting nucleic acid is fixed to a substrate and the double-stranded nucleic acid is formed by dropping on the substrate the single-stranded target nucleic acid, the other detecting nucleic acid and the receptor.

See 2144.04 Legal Precedent as Source of Supporting Rationale [R-6] - 2100 Patentability IV. CHANGES IN SIZE, SHAPE, OR SEQUENCE OF ADDING INGREDIENTS C. Changes in Sequence of Adding Ingredients. See *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is *prima facie* obvious.).

Regarding claims 19 and 20, Yoshimoto et al. teach wherein the receptor shows fluorescence emitting characteristics and the gene mutation is identified as a change of fluorescence strength of the double-stranded nucleic acid into which the receptor is inserted (see Fig. 4 where the receptor shows fluorescence emitting characteristics and

the gene mutation is identified as a change of fluorescence strength of the double-stranded nucleic acid into which the receptor is inserted).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Nakatani et al. in the method of Yoshimoto et al. The motivation to do so is provided to one of ordinary skill in the art by teachings of Nakatani et al. who state " We have developed a mismatch-detecting sensor useful for a surface Plasmon resonance (SPR) assay by immobilizing 2 (note added by Examiner 2 = naphthyridine compound) onto the dextran-coated gold surface." (see page 12651 col. 2 par. 2). They go on to teach its successful use in determining gene mutation. Hence one of ordinary skill in the art has a reasonable expectation of success in being able to develop a sensor for detecting mutations using the receptor (which is also a naphthyridine compound) taught by Yoshimoto et al., immobilizing it to a surface as taught by Nakatani et al. and be able to use surface plasmon resonance (SPR) technology to determine the nature of mutation.

Conclusion

11. All claims under consideration 12-20 are rejected over prior art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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